

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Anastasia G. Daifotis et al.

Serial No. 10/508,899

Filed: September 23, 2004

For: METHOD FOR INHIBITING BONE RESORPTION WITH  
AN ALENDRONATE AND VITAMIN D FORMULATION

Art Unit: Not Assigned

Examiner: Not Assigned

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR 1.97

Sir:

1. In compliance with 37 C.F.R. 1.97, submitted on the attached form herewith is a list of patents, publications or other information which are requested to be made of record in this application. This Information Disclosure Statement is not an admission that any patent, publication or other information referred to herein is "prior art" for this invention. In accordance with 37 C.F.R. 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. 1.56(b).

2. In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

3. Applicants respectfully request that the Examiner initial the attached form after reviewing the pertinence of each reference.

4. Pursuant to 37 C.F.R. 1.98 (a)(2)(ii), copies of each cited U.S. patent and each U.S. patent application publication are not enclosed herewith.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.

By

*Deanne Brown*

Date

*12/9/04*



## INFORMATION DISCLOSURE STATEMENT

5. Pursuant to 37 C.F.R. 1.98(d), copies of references listed on the attached form that were submitted to or cited - by the Office in a related application upon which the instant application relies for an earlier filing date under 35 U.S.C. 120 are not enclosed. Related application(s) in which references were submitted to or cited by the Office are as follows:

| RELATED APPLICATION |             |            |
|---------------------|-------------|------------|
| U. S. SERIAL NUMBER | FILING DATE | MERCK CASE |
|                     |             |            |
|                     |             |            |
|                     |             |            |
|                     |             |            |
|                     |             |            |
|                     |             |            |
|                     |             |            |

If this is inconvenient, additional copies will be submitted upon request.

6. In accordance with 37 C.F.R. 1.97, (check one)

- ☒ the attached information is filed within three months of the filing date of the captioned case.
- ☐ the attached information is filed more than three months after the filing date but prior to the mailing of a first Office Action on the merits.
- ☐ the attached information is being filed more than three months after the filing date and after the mailing of a first Office Action on the merits, but before the mailing date of a Final Action or Notice of Allowance. The enclosed authorization is therefore given to charge Deposit Account No. 13-2755 for the fee required under 37 C.F.R. 1.17(p).
- ☐ the undersigned certifies that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement.
- ☐ the undersigned certifies that no item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated under 37 C.F.R. 1.56(c) more than three months prior to the filing of this Statement.

Respectfully submitted,

By: Dianne Brown

Attorney \_\_\_\_\_ For Applicant(s)

Reg. No. 42,068

MERCK & CO., INC.

Patent Dept., RY60-30

P.O. Box 2000

Rahway, N.J. 07065-0907

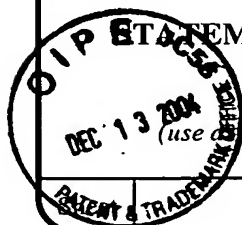
(732)594- 1249

Date: December 9, 2004

Substitute for form 1449A/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT



1 of 11

### COMPLETE IF KNOWN

Application Number 10/500,009  
 Filing Date September 23, 2004  
 First Named Inventor Anastasia G. Daifotis  
 Group Art Unit To be determined  
 Examiner Name To be determined  
 Attorney Docket Number 21001YP

### U.S. PATENT DOCUMENTS

| Examiner Initials* | Cite No. | U.S. Patent Document |                      | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
|--------------------|----------|----------------------|----------------------|---|--|
|                    |          | Number               | Kind Code (if known) |   |  |
|                    |          | 4,812,304            |                      | Anderson et al.                                 | 03/14/1989                                       |
|                    |          | 5,488,041            |                      | Barbier et al.                                  | 01/30/1996                                       |
|                    |          | 2003/0225039         |                      | Bauss et al.                                    | 12/04/2003                                       |
|                    |          | 5,358,941            |                      | Bechard et al.                                  | 10/25/1994                                       |
|                    |          | 5,882,656            |                      | Bechard et al.                                  | 03/16/1999                                       |
|                    |          | 5,583,122            |                      | Benedict et al.                                 | 12/10/1996                                       |
|                    |          | 4,876,248            |                      | Breliere et al.                                 | 10/24/1989                                       |
|                    |          | 5,780,455            |                      | Brenner et al.                                  | 07/14/1998                                       |
|                    |          | 5,616,571            |                      | Daifotis et al.                                 | 04/01/1997                                       |
|                    |          | 5,994,329            |                      | Daifotis et al.                                 | 11/30/1999                                       |
|                    |          | 6,225,294            |                      | Daifotis et al.                                 | 05/01/2001                                       |
|                    |          | 6,432,932            |                      | Daifotis et al.                                 | 08/13/2002                                       |
|                    |          | 2003/0139378         |                      | Daifotis et al.                                 | 07/24/2003                                       |
|                    |          | 5,622,721            |                      | Dansereau et al.                                | 04/22/1997                                       |
|                    |          | 2004/0053813 A1      |                      | DeLuca et al.                                   | 03/18/2004                                       |
|                    |          | 4,980,171            |                      | Fels et al.                                     | 12/15/1990                                       |
|                    |          | 6,281,381            |                      | Finkelstein et al.                              | 08/28/2001                                       |
|                    |          | 4,761,406            |                      | Flora et al.                                    | 08/02/1988                                       |
|                    |          |                      |                      |   |  |
|                    |          |                      |                      |   |  |

### FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. | Foreign Patent Document |                             | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
|--------------------|----------|-------------------------|-----------------------------|---|--|
|                    |          | Office                  | Number Kind Code (if known) |   |  |
|                    |          |                         | WO 92/21355                 | Andon   | 12/10/1992                                       |
|                    |          |                         | WO 95/08331                 | Bechard   | 03/30/1995                                       |
|                    |          |                         | JP 08-277223                | Chugai Pharmaceutical Co., Ltd.                 | 10/22/1996                                       |
|                    |          |                         | WO 03/086415                | Daifotis et al.                                 | 10/23/2003                                       |
|                    |          |                         | WO 90/01321                 | DeLuca et al.                                   | 02/22/1990                                       |
|                    |          |                         | WO 94/21242                 | D'Souza et al.                                  | 09/29/1994                                       |
|                    |          |                         | EP 0 274 158                | Ebetino et al.                                  | 07/13/1988                                       |
|                    |          |                         | WO 03/007916                | Fleshner-Barak et al.                           | 01/30/2003                                       |
|                    |          |                         | WO2004/058235               | Fleshner-Barak et al.                           | 07/15/2004                                       |
|                    |          |                         |                             |   |  |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449A/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

DEC 13 2004

(use many sheets as necessary)

### COMPLETE IF KNOWN

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/501,179            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001 YP              |

Sheet 2 of 11

### U.S. PATENT DOCUMENTS

| Examiner<br>Initials* | Cite<br>No. | U.S. Patent Document |                            | Name of Patentee or Applicant<br>of Cited Document | Date of Publication of<br>Cited Document<br>MM-DD-YYYY |
|-----------------------|-------------|----------------------|----------------------------|--|--|
|                       |             | Number               | Kind<br>Code<br>(if known) |  |  |
|                       |             | 4,822,609            |                            | Flora et al.                                       | 04/18/1989   |
|                       |             | 4,230,700            |                            | Francis et al.                                     | 10/28/1980   |
|                       |             | 4,330,537            |                            | Francis et al.                                     | 05/18/1982   |
|                       |             | 5,773,429            |                            | Fuisz  | 06/30/1998   |
|                       |             | 4,927,814            |                            | Gall et al.  | 05/22/1990   |
|                       |             | 5,616,560            |                            | Geddes   | 04/01/1997   |
|                       |             | 5,270,365            |                            | Gertz et al.                                       | 12/14/1993   |
|                       |             | 4,970,335            |                            | Isomura et al.                                     | 11/13/1990   |
|                       |             | 5,853,759            |                            | Katdare et al.                                     | 12/29/1998   |
|                       |             | 4,922,007            |                            | Kieczkowski et al.                                 | 05/01/1990   |
|                       |             | 5,019,561            |                            | Kieczkowski et al.                                 | 05/28/1991   |
|                       |             | 5,801,164            |                            | Knutson et al.                                     | 09/01/1998   |
|                       |             | 2003/0129194         |                            | Mazess et al.                                      | 07/10/2003   |
|                       |             | 4,425,339            |                            | Pitchford  | 01/10/1984   |
|                       |             | 4,621,077            |                            | Rosini et al.                                      | 11/04/1986   |
|                       |             | 5,227,506            |                            | Saari et al.                                       | 07/13/1993   |
|                       |             | 5,804,570            |                            | Santora II et al.                                  | 09/08/1998   |
|                       |             | 5,366,965            |                            | Strein et al.                                      | 11/22/1994   |
|                       |             |                      |                            |  |  |
|                       |             |                      |                            |  |  |

### FOREIGN PATENT DOCUMENTS

| Examiner<br>Initials* | Cite<br>No. | Foreign Patent Document |                 |                            | Name of Patentee or Applicant<br>of Cited Document | Date of Publication of<br>Cited Document<br>MM-DD-YYYY |
|-----------------------|-------------|-------------------------|-----------------|----------------------------|--|--|
|                       |             | Office                  | Number          | Kind<br>Code<br>(if known) |  |  |
|                       |             |                         | WO 94/00129     |                            | Francis et al.                                     | 01/06/1994   |
|                       |             |                         | WO 96/17616     |                            | Gazard et al.                                      | 06/13/1996   |
|                       |             |                         | WO 93/11786     |                            | Geddes et al.                                      | 06/24/1993   |
|                       |             |                         | EP 0 600 834 A1 |                            | Goodship et al.                                    | 06/08/1994   |
|                       |             |                         | WO 95/30421     |                            | Goodship et al.                                    | 11/16/1995   |
|                       |             |                         | EP 0128 736 A1  |                            | Hirata et al.                                      | 12/19/1984   |
|                       |             |                         | WO 01/97788     |                            | Horowitz et al.                                    | 12/27/2001   |
|                       |             |                         | WO 94/00130     |                            | Hovancik et al.                                    | 01/06/1994   |
|                       |             |                         |                 |                            |  |  |
|                       |             |                         |                 |                            |  |  |

Examiner  
Signature

Date  
Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

### STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

3

of

11

**COMPLETE IF KNOWN**

Application Number

10/50

**Filing Date**

September 23, 2004

**First Named Inventor**

Anastasia G. Daifotis

## Group Art Unit

To be determined

Examiner Name

To be determined

Attorney Docket Number

21001YP

[illegible]

| Examiner Initials* | Cite No. | Foreign Patent Document |                 |                         | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document<br>MM-DD-YYYY |
|--------------------|----------|-------------------------|-----------------|-------------------------|---|---|
|                    |          | Office                  | Number          | Kind Code<br>(if known) |   |   |
|                    |          |                         | JP 11-60489     |                         | Ito et al.                                      | 03/01/1999  |
|                    |          |                         | WO 01/28564 A1  |                         | Kang et al.                                     | 04/26/2001  |
|                    |          |                         | WO 96/25166     |                         | Karpf et al.                                    | 08/22/1996  |
|                    |          |                         | WO 95/29679     |                         | Katdare et al.                                  | 11/09/1995  |
|                    |          |                         | HU P9403762     |                         | Proctor & Gamble Pharma., Inc.                  | 09/28/1995  |
|                    |          |                         | EP 1 051 976 A2 |                         | Roldan et al.                                   | 11/15/2000  |
|                    |          |                         | WO 95/28145     |                         | Shinoda et al.                                  | 10/26/1995  |
|                    |          |                         |                 |                         |   |   |
|                    |          |                         |                 |                         |   |   |
|                    |          |                         |                 |                         |   |   |

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449A/PTO

## INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

(use ~~as~~ many sheets as necessary)

Sheet

4

of

11

Attorney Docket Number

21001YP

**COMPLETE IF KNOWN****Application Number**

10/50 9

**Filing Date**

September 23, 2004

**First Named Inventor**

**Anastasia G. Daifotis**

### Group Art Unit

To be determined

Examiner Name

**To be determined**

## U.S. PATENT DOCUMENTS

[illegible]

## FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. | Foreign Patent Document |                 |                      | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
|--------------------|----------|-------------------------|-----------------|----------------------|---|--|
|                    |          | Office                  | Number          | Kind Code (if known) |   |  |
|                    |          |                         | JP 64-00021     |                      | Teijin Ltd.                                     | 01/05/1989                                       |
|                    |          |                         | BE 672205       |                      | The Proctor & Gamble Company                    |  |
|                    |          |                         | WO 99/20635     |                      | Tomer   | 04/29/1999                                       |
|                    |          |                         | JP 07-330613    |                      | Tsuchimoto et al.                               | 12/19/1995                                       |
|                    |          |                         | EP 0162510      |                      | Uchtman   | 08/28/1991                                       |
|                    |          |                         | EP 0 381 296 B1 |                      | Uchtman   | 11/30/1994                                       |
|                    |          |                         | WO 95/28936     |                      | Yates   | 11/02/1995                                       |
|                    |          |                         | WO 96/38156     |                      | Yates   | 12/05/1996                                       |
|                    |          |                         |                 |                      |   |  |
|                    |          |                         |                 |                      |   |  |

Examiner  
Signature

Date  
Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**SEND TO:** Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449B/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

(use as many sheets as necessary)

### COMPLETE IF KNOWN

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,009            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001YP               |

Sheet 5 of 11

### NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.   |
|--------------------|----------|--|
|                    |          | Actonel™ (risedronate sodium tablets) package insert, dated March 1998.  |
|                    |          | Adachi, Today's Therapeutic Trends, Vol. 14, No. 1 (1996), pp. 13-24, "Osteoporosis -- its diagnosis, management and treatment with a new oral bisphosphonate agent, etidronate".  |
|                    |          | Affidavit of Gideon Rodan from validity trial of IL 94612 dated 17 Nov. 2000   |
|                    |          | Ammann, P., et al., J. Bone Miner. Res., 1993, Vol 8(12), pp. 1491-8   |
|                    |          | Augsburger, L. L., et al., J. Pharm Aci, 1996, Vol. 55, p 418  |
|                    |          | Balena et al., J. Clin. Invest., Vol. 92 (1993), pp. 2577-2586, "The effects of 2-year treatment with the aminobisphosphonate alendronate on bone metabolism, bone histomorphometry, and bone strength in ovariectomized nonhuman primates". |
|                    |          | Balena et al., Bone, 1993, Vol. 14, pp. 499-504, "The Aminobisphosphonate Alendronate inhibits bone loss induced by thyroid hormone in the rat comparison between effects on tibiae and vertebrae."  |
|                    |          | Bankhurst et al., Arthritis and Rheumatism, Vol. 38, No. 9, Suppl. 1 (1995), S359, "Three-year treatment with alendronate prevents fractures in women with postmenopausal osteoporosis".   |
|                    |          | Baran, Geriatrics, Vol. 56, No. 3 (March 2001), pp. 28-32, "Osteoporosis: Efficacy and safety of a bisphosphonate dosed once weekly".  |
|                    |          | Bell et al., Endocrine, Vol. 6(2) (1997), pp. 203-206, "Bisphosphonates in the Treatment of Osteoporosis".   |
|                    |          | Binkley et al., J. Clin. Endo. & Metab., 2004, Vol. 89(7), pp. 3152-3157.  |
|                    |          | Black D.M. et al., The Lancet, 1996, 348, 1535-1541  |
|                    |          | Blank, American College of Gastroenterology 66th Annual Scientific Meeting, "Lack of gastric adaptation to weekly versus daily alendronate administration in rats".  |
|                    |          | Bone et al., Clinical Therapeutics, Vol. 22, No. 1 (2000), pp. 15-28, "Weekly administration of alendronate: Rationale and plan for clinical assessment".  |
|                    |          |  |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449B/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

COMPLETE IF KNOWN

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,899            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001YP               |

Sheet 6 of 11

(use as many sheets as necessary)

### NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.   |
|--------------------|----------|--|
|                    |          | Bone et al., Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), M392, "Once-weekly alendronate: Two year subgroup efficacy analyses in postmenopausal women with osteoporosis".                                 |
|                    |          | Bone III et al., 6th International Symposium on Clinical Disorders of Bone and Mineral Metabolism, Venice, Italy, November 20-25, 1999, "Alendronate 70 mg once weekly is therapeutically equivalent to alendronate in 10 mg daily". |
|                    |          | Bonjour, J-P, , Endocrinol. Metab., 1988, Vol. 17, pp. E260-E264   |
|                    |          | Brown et al., Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), M402, "Efficacy, safety and tolerability of once weekly (80 mg vs. 160 mg) oral alendronate in postmenopausal osteoporosis".                   |
|                    |          | Cassidy et al., Digestive Diseases and Sciences, Vol. 37 (1992), pp. 1206-1211, "Continuous versus intermittent acid exposure in production of esophagitis in feline model".   |
|                    |          | Castell, (an editorial), N. England J. of Medicine (1996), Vol. 335, pp. 1058-1059, "Pill esophagitis - the case of alendronate".  |
|                    |          | Chen, T. C., et al., J. Nutr. Biochem., 1990, Vol. 1, pp. 272-276, "A method for the determination of the circulating concentration of vitamin D"  |
|                    |          | Chesnut et al., Am. J. of Medicine, Vol. 99 (1995), pp. 144-152, "Alendronate treatment of the postmenopausal osteoporotic woman ...".   |
|                    |          | Chesnut et al., Osteoporosis Int'l (1993), Suppl. 3: S17-19, "Short-term effect of alendronate on bone mass and bone remodeling in postmenopausal women".  |
|                    |          | De Groen et al., N. England J. of Medicine, (1996), Vol. 335, pp. 1016-1021, "Esophagitis associated with the use of alendronate"  |
|                    |          | Delaney et al., ENDO 2001, The Endocrine Society's 83rd Annual Meeting, Denver, Colorado (June 2001), Abstract, P1-469 (June 2001), p. 249, "Bone density changes in response to risedronate once weekly"                            |
|                    |          | de Vernejoul et al., Calcified Tissue Int'l, Vol. 40 (1987), pp. 160-165, "Different schedules of administration of (3 amino-1-hydroxypropylidene)-1,1-bisphosphonate induce different changes ..."                                  |
|                    |          | Devogelaer et al., Bone, 1996, Vol.18(2), pp. 141-150, "Oral alendronate induces progressive increases in bone mass of the spine, hip and total body over 3 years in postmenopausal women with osteoporosis."                        |
|                    |          | Dhesi, J.T., et al., Age and Aging, 2002, Vol. 31, pp. 267-271   |
|                    |          |  |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003



Substitute for form 1449B/PTO

# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use many sheets as necessary)

**COMPLETE IF KNOWN**

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,000            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001YP               |

Sheet 7 of 11

## **NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.  |
|--------------------|----------|---|
|                    |          | Dukas, L., et al., JAGS, 2004, Vol. 52, pp. 230-236   |
|                    |          | E-mail communication of February 20, 1998 from Melton to DiCesare et al.  |
|                    |          | Exton-Smith, A.N., et al., Lancet, 1966, Vol. 2, pp. 999-1001   |
|                    |          | Filipponi et al., J. of Bone & Min. Research, Vol. 10 (1995), pp. 697-703, "Cyclical clondronate is effective in preventing postmenopausal bone loss: A comparative study with transcutaneous hormone replacement therapy". |
|                    |          | Fleisch, J. of Clin. Endoc. & Metab., Vol. 76 (1993), pp. 1397-1398, "Editorial: Prospective use of bisphosphonates in osteoporosis".   |
|                    |          | Fleisch H., Bisphosphonates in Bone Disease from the Laboratory to the patient, 1995 Book   |
|                    |          | Fleisch, Expert Opinion Therapeutic Patents, Vol. 11, No. 9 (2001), p. 1371-1381, "Bisphosphonates: mechanisms of action".  |
|                    |          | Fleisch et al. Hormone and Metabolic Research, Vol. 29 (1997), pp. 145-150, "Bisphosphonates: Mechanisms of action and clinical use in osteoporosis - an update."   |
|                    |          | Fleisch et al., Bisphosphonates in Bone Disease, From the laboratory to the patient, 4th edition, Academic Press (2000) Book  |
|                    |          | Fleisch, Osteoporosis Int., 1996, Vol. 6, pp. 166-70  |
|                    |          | Frediani et al., Clin Drug Invest., 1998, Vol. 15(3), pp. 235-244, "Effects of combined treatment with calcitriol plus alendronate on bone mass turnover in postmenopausal osteoporosis two years of continuous treatment." |
|                    |          | Gallagher, J.C., et al., J. Clin. Endocrinol. Metab., 1980, Vol. 51(6), pp. 1359-64   |
|                    |          | Gertz et al., Clin. Pharmacology & Ther. (1995), Vol. 58, pp. 288-98, "Studies of the oral bioavailability of alendronate"  |
|                    |          |   |
|                    |          |   |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449B/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

(use as many sheets as necessary)

COMPLETE IF KNOWN

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,000            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001YP               |

8 of 11

### NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.  |
|--------------------|----------|---|
|                    |          | Gertz et al., J. of Bone & Min. Res., Vol. 6, Suppl. 1 (1991), Abstract No. 790, p. S281, "Oral bioavailability and dose proportionality of alendronate (aminohydroxybutylidene bisphosphonate) in postmenopausal women". |
|                    |          | Gertz et al., J. of Bone & Min. Res., Vol. 9 (1994), pp 135-142, "Monitoring bone resorption in early postmenopausal women by an immunoassay for cross-linked collagen peptides in urine".                                |
|                    |          | Gertz et al., Osteoporosis Int. (1993), Suppl. 3: S13-16, "Clinical pharmacology of alendronate sodium"   |
|                    |          | Gordon et al., ENDO 2001, The Endocrine Society's 83rd Annual Meeting, Denver, Colorado (June 2001), Abstract, P1-460 (June 2001), p. 247, "Weekly administration of risedronate increase bone mineral density".          |
|                    |          | Haden, S. T., et al., Calcif Tissue Int., 1999, Vol. 64, pp.275-279   |
|                    |          | Harris et al., J. of Clin. Endoc. & Metab., 76:1399-1406 (1993), "The effect of short term treatment with alendronate on vertebral density and biochemical markers of bone..."  |
|                    |          | Heaney et al., Osteoporosis Int., 2000, Vol. 11, pp.553-5   |
|                    |          | Holzherr, M. L., et al., Osteoporosis Int., 2000, Vol. 11, pp.43-51   |
|                    |          | Khan et al., Bone, Vol. 20 (1997), pp. 263-271, "Alendronate in the treatment of Paget's disease of bone".  |
|                    |          | Latham et al., JAGS, 2003, Vol. 51, pp. 1219-1226   |
|                    |          | Lerk, C. F., et al., Pharm. Acta. Helv., 1977, Vol., 52, Nr 3, pp. 33-39  |
|                    |          | Liberman et al., (correspondence), N. England J. of Medicine (1996), Vol. 335, pp. 1069-1070, "Esophagitis and alendronate".  |
|                    |          | Liberman et al., N. Eng. J. of Medicine, Vol. 333 (1995), pp. 1437-1443, "Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis".                              |
|                    |          | Lindsay et al., Arthritis & Rheumatism, Vol. 44, No. 9 (Suppl.), Abstract No. 604, "Risedronate 35 mg once a week is as effective as 5 mg daily in postmenopausal women".   |
|                    |          |   |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449B/PTO

# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(use as many sheets as necessary)

**COMPLETION IF KNOWN**

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,799            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001YP               |

Sheet 9 of 11

## **NON PATENT LITERATURE DOCUMENTS**

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.  |
|--------------------|----------|---|
|                    |          | Lombardi et al., Ann. Ital. Med. Int. 7, 1992, 3 Suppl., 158-165  |
|                    |          | Lufkin et al., Osteoporosis Int'l. (1994), Vol. 4, pp. 320-322, "Pamidronate: An unrecognized problem in gastrointestinal tolerability".  |
|                    |          | Lunar News, April 1997, "Update: Bisphosphonate", pp. 30-32   |
|                    |          | Lunar News (April 1996), "Update: Bisphosphonate", p. 31  |
|                    |          | Lunar News (July 1996), "Update: Bisphosphonate", pp. 23-24   |
|                    |          | Matsumoto, K., et al., Biochimica et Biophysica Acta, Vol. 1092 (1992), pp. 311-318   |
|                    |          | McClung et al., Bone, Vol. 17 (1995), pp. 493S-496S, "Tiludronate therapy for Paget's disease of bone".   |
|                    |          | McKenna, M. J., Am. J. Med, 1992, Vol. 93, pp.69-77   |
|                    |          | Melsen et al., Osteoporosis, Chapt. 60(1996), pp. 1145-1158, "ADFR - The Concept and its performance".  |
|                    |          | Men's Osteoporosis Support Group, Vol. 1, Issue 2, 1 July 1997  |
|                    |          | Merck & Co., Inc. - Instructions for Once Weekly Fosamax, January 2001  |
|                    |          | Mortensen et al., J. Bone & Min. Res., (1995), 10 (Supp. 1): S360, "Prevention of early postmenopausal bone loss by residronate: A two year study".   |
|                    |          | Mortensen et al., J. of Bone & Mineral Res., (1995) Vol. 10, suppl. 1, p. s140, "Prevention of early postmenopausal bone loss of risedronate".  |
|                    |          | Passeri et al., Bone and Mineral, 1991, Vol. 15, pp. 237-248, "Intermittent treatment with intravenous 4-amino-1-hydroxybutlidene-1,1-bisphosphonate (AHBuBP) in the therapy of postmenopausal osteoporosis." |
|                    |          | Peter et al., Digestive Diseases & Sciences, Vol. 43 (1998), pp. 1009-1015, "Comparative study of potential for bisphosphonates to damage gastric mucosa of rats".  |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449B/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

(use as many sheets as necessary)

COMPLETELY KNOWN

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,000            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001YP               |

Sheet 10 of 11

### NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.  |
|--------------------|----------|---|
|                    |          | Peter et al., Digestive Diseases & Sciences, Vol. 43 (1998), pp. 1998-2002, "Esophageal irritation due to alendronate sodium tablets".  |
|                    |          | Peter et al., Journal of Pharmacology & Experimental Therapeutics, Vol. 276, No. 1 (1996), p. 271-276, "Long-term safety of the aminobisphosphonate alendronate in adult dogs".                                       |
|                    |          | Physician's Desk Reference, 51st ed. (1997), pp. 1703-1706, "Fosamax".  |
|                    |          | Reddy M.S. et al, J. Periodontol, 1995, Vol. 66(3), 211-217   |
|                    |          | Reid et al., American Journal of Medicine, 1996, Vol. 101, pp. 341-348, "Biochemical and radiologic improvement in Paget's disease of bone treated with alendronate: a randomized, placebo-controlled trial           |
|                    |          | Reszka et al., Curr. Rheumatol. Rep., Vol. 5(1), pp. 65-74 (2003), "Bisphosphonate mechanism of action."  |
|                    |          | Reszka et al., Mol. Pharmacol., 2001, Vol. 59(2), pp. 193-202   |
|                    |          | Rizzoli et al., Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), M401, "Two year results of once-weekly administration of alendronate 70 mg for the treatment of postmenopausal osteoporosis"  |
|                    |          | Rodan et al., Osteoporosis International (1993) Suppl., 3:S7-12, "Preclinical Pharmacology of alendronate"  |
|                    |          | Rote List 1997, 66 023 (Fosamax)  |
|                    |          | Schnitzer et al., Aging: Clinical and Experimental Research, Vol. 12, No. 1 (2000), P. 1-12, "Therapeutic equivalence of alendronate 70 mg once-weekly and alendronate 10 mg daily in the treatment of osteoporosis". |
|                    |          | Schnitzer, Expert Opinion Pharmacother., Vol. 2, No. 9 (2001), pp. 1461-1472, "Update on alendronate for osteoporosis: once-weekly dosing".   |
|                    |          | Scrip (11/24/99), "Merck develops once-weekly Fosamax   |
|                    |          | Seedor et al., Journal of Bone & Mineral Research, Vol. 6, No. 4 (1991), pp. 339-346, "The bisphosphonate alendronate (MK-217) inhibits bone loss due to ovariectomy in rats".  |
|                    |          |   |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003

Substitute for form 1449B/PTO

# INFORMATION DISCLOSURE

## STATEMENT BY APPLICANT

DEC 13 2004

(use as many sheets as necessary)

COMPLIANCE IF KNOWN

|                        |                       |
|------------------------|-----------------------|
| Application Number     | 10/508,409            |
| Filing Date            | September 23, 2004    |
| First Named Inventor   | Anastasia G. Daifotis |
| Group Art Unit         | To be determined      |
| Examiner Name          | To be determined      |
| Attorney Docket Number | 21001 YP              |

Sheet 11 of 11

### NON PATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. | Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.   |
|--------------------|----------|--|
|                    |          | Seltenmeyer et al., Bone (NY), Vol. 20, No. 4, Suppl., (1997) pp. 114S, "A comparison of the antiresorptive potency of various bisphosphonates in vivo with their inhibitory effect in vitro on squalene synthase and cellular sterol synthesis".            |
|                    |          | Singer et al., Advances in Endocrin.& Metab., Vol. 6 (1995), pp. 259-288, "Bisphosphonates in the treatment of disorders or mineral metabolism".   |
|                    |          | Siris et al, J. Clin. Endo. Metab., 1996, Vol. 81(3), pp. 961-967, "Comparative study of alendronate versus etidronate for the treatment of Paget's disease of bone."  |
|                    |          | Sorrentino, Endoscopy, Vol. 28 (1996), p. 529, "Esophageal ulceration due to alendronate".   |
|                    |          | Strumpf et al., Histochemistry, 1987, Vol. 87(1), pp.53-58   |
|                    |          | The Pink Sheet (Dec. 18, 1995), Vol. 57, Issue 51, "Merck Cozaar generating 25,000 scripts weekly after six months on market; Fosamax off to quick start, company tells securities analyst meeting".   |
|                    |          | Thompson et al., J. of Bone & Min. Research, Vol. 7(1992), pp. 951-960, "The bisphosphonate, alendronate, prevents bone loss in ovariectomized baboons".   |
|                    |          | Toolan et al., J. Bone Min. Res., 1992, Vol. 7, pp. 1399-1406, "Effects of 4-amino-1-hydroxybutylidene bisphosphonate on bone biomechanics of rats."   |
|                    |          | Van Dyke, et al., Annals of the Rheumatic Diseases, Annual European Congress of Rheumatology, EULAR 2001, Prague, Czech Republic, Vol. 60, Suppl. 1 (July 2001), Abstract SAT0167, p. 256, "Safety of once-weekly alendronate 70 mg in periodontal disease". |
|                    |          | Vasikaran, S. D., Ann. Clin. Biochem., (2001) Vol. 38, pp. 608-623, "Bisphosphonates: An overview with special reference to alendronate."  |
|                    |          | Vreeken, R. J., et al., Biological Mass Spectrometry, 1993, Vol. 22, pp. 621-632,  |
|                    |          | Wimalawansa, ENDO 2001, The Endocrine Society's 83rd Annual Meeting, Denver, Colorado (June 2001), Abstract P1-438, p. 241-242, "Highly efficacious and cost-effective alendronate regimen for postmenopausal osteoporosis: A four-year clinical study"      |
|                    |          | Wimalawansa, Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), Abstract SA352, "Once a week alendronate therapy: A convenient and effective way of prevention and treatment of osteoporosis: A four-year clinical study".              |
|                    |          | Wimalawansa, Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), Abstract SU399, "Efficacy of once a week risedronate in comparison with once-weekly alendronate therapy for postmenopausal osteoporosis: One-year data                  |
|                    |          | Woodson, Osteoporosis International, Vol. 11, Suppl. 2 (2000), Chicago, Illinois, p. S204, Abstract 550 (514), "Once weekly risedronate therapy".  |

Examiner Signature

Date Considered

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

SEND TO: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450. Computer generated form "IDS Form" (IDS Folder), Merck & Co., Inc., 09/05/2003